

DOCKET NO.: ISIS-1158

**RESPONSE UNDER 37 CFR 1.116
EXPEDITED PROCEDURE
EXAMINING GROUP 1631**

In claim ~~47~~, in line 37 thereof, delete "R3" and substitute --R³-- therefor.

In claim 33, in the second line thereof, delete "R¹³" and substitute --R¹²-- therefor.

REMARKS

Claims 1, 5, 8-10, 12, 13, 15, 20, 22-24, 30-33, 37 and 39-50 are pending in this application. Applicants thank the Examiner for indicating that claims 12, 13, 39, 41, 44, 46 48 and 49 are allowed.

Applicants thank the Examiner for the helpful comments on page 2 of the present Office Action. Applicants confirm that claims 12 and 13 were intended to depend from claim 39, and that in claim 32, Applicants indeed intended to delete "R¹² is a conjugate".

Claims 30-33 and 47 are rejected under 35 U.S.C. §112, second paragraph, for lack of correct superscripting. In response, Applicants have amended the claims to introduce appropriate superscripting into claims 30 and 47, thus overcoming the rejection.

Claim 33 is rejected under 35 U.S.C. §112, fourth paragraph, for failing to further limit claim 30. In response, claim 33 has been amended to recite that R¹² is a conjugate, thus overcoming the rejection.

The Office Action has maintained its rejection of claims 1, 8, 15, 20, 22-24, 37, 40, 42 45 and 50 under 35 U.S.C. § 103(a) as being unpatentable over Publication WP 93/12129 to Thompson et al. ("Thompson et al.") on the basis that Thompson et al. discloses an amino linked terminal blocking group "Q" at

pages 5-6 thereof, which can be a steroidal moiety. Applicants respectfully request reconsideration of the rejection.

The Office Action asserts that the priority document, PCT/EP92/01219, does not disclose "steroidal Q entities as given in Thompson et al." However, as Applicants stated in their prior response, the priority document, PCT/EP92/01219 discloses that the terminal moiety (denotes as groups Q or I in the formulas described therein) can bear ligands. See page 17 of PCT/EP92/01219 at, for example, lines 3-12. Such "I" groups are described at page 9, line 26, to include steroids. Accordingly, the priority document discloses the terminal steroidal moieties of the Thompson et al. reference. Thus, the disclosure of terminal steroid groups Thompson et al. is not a proper basis for rejection of the present claims under 35 U.S.C. § 103(a). See *In re Stryker*, 168 U.S.P.Q. 372 (C.C.P.A. 1971).

The Office Action also appears to assert that the priority document only discloses species that contain blocked amino termini. However, the priority document clearly describes the preparation of such unblocked species at, for example, page 57, line 26 et seq. Inasmuch as the Priority document discloses the pertinent disclosure of Thompson et al. reference, Applicants respectfully request reconsideration and withdrawal of this rejection.

The Office Action has maintained its rejection of claims 1, 8, 15, 20, 37 and 40 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,834,607 to Manoharan et al. ("Manoharan et al.") in view of Nielsen et al., Science 254:1497 (1991) ("Nielsen et al."). Applicants will submit within in due course a declaration of Dr. Manoharan attesting to the fact that

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he alone invented the subject matter that the Office Action asserts renders the present claims obvious when combined with the Nielsen disclosure. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

The Office Action has maintained its rejection of claims 1, 5, 8-10, 15, 20, 22-24, 30-33, 37 40, 42, 43, 45 and 50 under 35 U.S.C. § 103(a) as being unpatentable over either Thompson et al. or Manoharan et al. taken in view of Nielsen et al., further taken in view of U.S. Patent No. 4,711,955 to Ward et al. ("Ward et al."). Inasmuch as both primary references (i.e., the Thompson et al. and the Manoharan et al. reference) are not prior art against the present claims as discussed above, Applicants respectfully request reconsideration and withdrawal of this rejection.

In view of the foregoing, Applicants submit that the claims presently before the Examiner patentably define the invention over the applied art and are otherwise in condition for ready allowance. An early Office Action to that effect is, therefore, earnestly solicited.

Respectfully submitted,


Michael P. Straher
Registration No. 38,325

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WOODCOCK WASHBURN KURTZ
MACKIEWICZ & NORRIS
One Liberty Place - 46th Floor
Philadelphia, PA 19103
(215) 568-3100